PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference LH/VB60671	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2005/000443	International filing date *(day/month/year)* 13.01.2005	Priority date *(day/month/year)* 16.01.2004
International Patent Classification (IPC) or national classification and IPC INV. C12N15/85		
Applicant GLAXO GROUP LIMITED et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of two sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03.04.2006	01.06.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Lonnoy, O Telephone No. +31 70 340-4294

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2005/000443

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-27	as originally filed

Sequence listings part of the description, Pages

1-4	received on 10.05.2005 with letter of 09.05.2005

Claims, Numbers

1-8, 10-22	filed with the demand
9	filed during an interview on 16.05.2006

Drawings, Sheets

1/12-12/12	as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 18,20 (industrial applicability)

because:

☒ the said international application, or the said claims Nos. 18,20 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*.

☐ no international search report has been established for the said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-22
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-22
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-17,19,21-22
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ on paper

   ☒ in electronic form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed

   ☐ filed together with the international application in electronic form

   ☒ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

   see separate sheet

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

I. Basis (Continuation)

- The statement that the written and electronic sequence listings subsequently filed to this I.S.A. do not include matter which extend beyond the content of the application as filed is missing. Since filing of said statement is a legal requirement, the sequence listings might be considered as not having been validly filed.

- During a telephone interview held on 16/05/2006, the Applicant requested amendment of claim 9, in the claim set filed with the Demand, to read as follows: "A polynucleotide vector comprising a promoter having the R2 enhancer element of the HCMV US3 gene promoter, and a minimal promoter element from a non-HCMV US3 gene promoter, the promoter being operably linked to a region encoding a tumor-associated antigen, self antigen or antigen derived from a pathogen which is foreign with respect to the HCMV US3 protein". Basis being found e.g. on p.6 ln.3, p.8 ln.32, p10 ln.30 and p.4 ln.9-10.

III. Non-establishment of opinion (Continuation)

Claim 18, and claim 20 as far as the latter relates to a method practised in vivo, relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated in respect of the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

V. Reasoned statement (Continuation)

1. CITATIONS

Reference is made to the following documents:

D1: Chan Y-J et al (1996) J.Virol. vol.70, pp.5312-5328.

D3: Ertl PF et al (2003) Methods : a Companion to Methods in Enzymology, vol. 31, pp.199-206, XP004457832 ISSN: 1046-2023

D4: Thrower A et al (1996) J. Virol., vol.70, pp.91-100.

2. NOVELTY (Art. 33(2) PCT)

2.1. Claims 1-22 satisfy the criterion set forth in Article 33(2) PCT because the prior art as defined in the regulations (Rule 64(1)-(3) PCT) does not appear to disclose HCMV US3 gene promoter element operably linked to a region encoding a tumor-associated antigen, self antigen or antigen derived from a pathogen which is foreign with respect to the HCMV US3 protein.

3. INVENTIVE STEP (Art. 33(3) PCT)

3.1. The present application does satisfy the criterion set forth in Article 33(3) PCT, the subject-matter of claims 1-22 involving an inventive step (Art.33(3) PCT and R.65(1)(2) PCT), for the following reasons: D3, a review article on DNA vaccine vectors, can be considered to represent the

closest prior art. Most common DNA vaccine vectors are hCMV Mie promoter-based constructs, alternative promoters mentioned being the SV40-, RSV-, beta-actin-, and alpha-globin-promoters. No mention nor suggestion of the HCMV US3 gene promoter is made in D3. The objective problem underlying the application is the provision of an alternative promoter suitable for antigen expression in nucleic acid immunisation. The proposed solution is to rely on HCMV US3 gene promoter elements, to direct expression of the tumor-associated antigen, self antigen or antigen derived from a pathogen which is foreign with respect to the HCMV US3 protein. Said solution can be considered to involve inventive activity.for the following reasons: HCMV US3 promoter elements were characterised in the prior art (e.g. D1, D4). However, no document could be found in the prior art to suggest their usefulness in driving expression of a tumor-associated antigen, self antigen or antigen derived from a pathogen which is foreign with respect to the HCMV US3 protein. HCMV US3 promoter element-based vectors are shown in the application to yield expression levels in dendritic cells higher than e.g. SV40-promoter based vector (see e.g. example 3) and, most importantly, to induce antigen-specific CTL responses in mice and in pigs that are comparable to those induced by vectors based on the HCMV Major immediate early promoter (see e.g. figures 5 and 7-12). HCMV US3 promoter element-based vectors thus appear to be suitable alternatives to HCMV Mie promoter-based vectors, at least for antigen expression in DNA immunisation.
The US3 R1 silencer-element is an optional technical feature of the solution to said problem: D4 teaches (e.g. at Figure 1c) that a promoter holding the R1 silencer element is still active, albeit to a lower level than in absence of said silencer. Thus, said R1 enhancer element enables the skilled person to tailor transcription levels according to his needs, by deciding to include said silencer in his expression construct, or to omit it.
Finally, the skilled person would know how to reduce the subject-matter of claim 9 to practice, since transfer of the enhancer activity of the US3 R2 region to a heterologous promoter is known from the prior art (e.g. D1 p.5317 col.1 par.1).

4. INDUSTRIAL APPLICABILITY (Art. 33(4) PCT)

4.1. For the assessment of present claim 18, and of claim 20 as far as it relates to a method practised in vivo, on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.